REMARKS

I. Overview

Claims 5-33, and 99 have been canceled. Claims 1- 2, 34-65, 67-74, 85, and 102 have been amended to include the nucleotide sequence of the retroviral vector obtained from the plasmid of SEQ ID NO: 1. Claims 1-2, 34-65, 67-74, 85 and 102 have been amended to clarify that the nucleotide sequence introduced into the cells is not the nucleotide sequence of plasmid of SEQ ID NO: 1, but instead is the nucleotide sequence that results from reverse transcription and integration of the retroviral vector derived from plasmid of SEQ ID NO: 1. Support for these amendments may be found in the published specification 20040191229 at paragraphs 72, 127,141, 202 and 203 and Figures 1 and 2 as originally filed. No new matter has been added. Upon entry of this amendment, claims 1-4, 34-74, 85 and 100-103 are pending. In response to the Office Action from the Examiner dated July 27, it is respectfully requested that this Amendment After Final be entered and made of record. No new matter is presented, as such the Amendment is proper under 37 C.F.R. §1.121. Applicants' response is an earnest effort to place the pending claims and application in condition for allowance. Reconsideration and passage to issuance is therefore respectfully requested.

II. Support for Introduced Amendments

In response to the Examiner's interviews conducted on October 28, 2009 and November 24, 2009, during which claim amendments were discussed, the Examiner indicated that an amendment to the independent claims that describes the sequence introduced into the tumor cells that encodes an α(1,3)galactosyltransferase protein would potentially put the claims in form for allowance so long as the sequence is novel and is described with a reasonable degree of clarity.

Claims 1, 2, 67-74, 85 and 102 have been amended to recite in part "...the nucleotide sequence of a retroviral vector obtained from the plasmid of SEQ ID NO:1". Support for this amendment may be found throughout the specification, for example, at paragraphs 74, 130, 143, 144 and Figures 1 and 2. Applicants respectfully submit that the present amended claims are definite for the reasons set forth below and that a person of skill in the art would be able to understand the meaning of "...the nucleotide sequence of a retroviral vector obtained from the plasmid of SEQ ID NO:1" and the identity of the nucleotide sequence transferred into the recipient tumor cells.

As shown in Figure 1 and described in Example 1, for example, paragraph 143, plasmid pLNCKG is derived from pLNCX (Genbank Accession # M28247) publically available prior to Applicants' filing date. As support, Applicants submit herewith a copy of the entry from NCBI's Entrez Gene database associated with Genbank Accession # M28247 and the article referenced in Applicants' published patent application at paragraph 130, Miller, et al., Biotechniques. 7:980-990. (1989). See also the Information Disclosure Statement.

As disclosed in the Miller publication, pLNCX contains the 5' LTR from MoMSV, and the 3'LTR from MoMLV. Each one of these LTRs is divided into 3 regions named U3, R and U5. The structure of the 5'LTR in terms of the nucleotide numbers of SEQ ID No 1 is: U3 (nt 1-443), R (nt 444-513) and U5 (nt 514-589). The structure of the 3'LTR in terms of the nucleotide numbers of SEQ ID NO:1 is: U3 (nt 4605-5053), R (nt 5054-5121) and U5 (5122-5198).

The sequence of the LTR's was known prior to Applicants' filing date. For example, GenBank: X05161.1 provides the sequence of the 3'LTR from MoMLV, with description of the sequence for the U3-R-U5 subregions. GenBank: X05157.1 describes the sequence and subregions of 5'LTR MoMLV. See IDS submitted herewith containing the entries from NCBI's Entrez Gene database associated with Genbank Accession # X05161.1 and X05157.1. Using standard techniques such as sequence alignment, the nucleotide sequences present in SEQ ID NO:1 that correspond to the 5'LTR of MoMSV and 3'LTR MoMLV can be determined.

As described in Chapter 4 of Retroviruses, Ed John Coffin, Stephen Huges and Harold Varmus, 1997, Cold Spring Harbor Laboratory Press, pages 121-135, a copy of which is submitted herewith and also cited on an Information Disclosure Statement, it is well known in the art that transcription of retroviral RNA starts at the 5' end of the 5'R region and ends at the 3' end of the 3'R. See, pages 121-122 of Chapter 4.

Plasmid pLNCKG of SEQ ID NO:1 is the source of the retroviral vector that will be integrated into the target cell lines. To achieve this, Example 1 describes that pLNCKG is transfected into 293T.AMIZ vector producer cell line. In this cell line, the plasmid will direct transcription of retroviral RNA. Therefore, the sequence of the retroviral RNA present in retroviral vector particles will be nucleotides 444 to 5121 of SEQ ID NO:1 (plus addition of a polyA tail of variable length, that will not be part of the final integrated sequence). Upon transduction of these retroviral particles onto the target cells (Example 2 and Example 12, paragraphs 144, 190-191 of the published specification), the process of reverse transcription of the retroviral vector RNA into double stranded DNA and integration of the viral DNA into the host genomic DNA will take place. The process of reverse transcription is well described in the art (Retroviruses, Ed John Coffin, Stephen Huges and Harold Varmus, 1997, Cold Spring Harbor

Laboratory Press, ISBN 0-87969-497-1, Chapter 4, pages 121-136) and it involves the duplication of sequences from the 3'U3 into the 5'U3 and the 5'R-U5 into the 3'R-U5. Therefore, the nucleotide sequence of the retroviral vector derived from the plasmid of SEQ ID NO:1 that will be comprised within the human tumor cell line of the present invention will have the structure of: 3'U3-5'R-5'U5-NeoR-CMV-aGalT-3'U3-5'R-5'U5. This means that the nucleotide sequence of the retroviral vector obtained from plasmid of SEQ ID NO:1 will be (in terms of the nucleotide sequence of plasmid of SEQ ID No1): 5'-[4605-5053]-[444-5053]-[444-589]-3'. One of ordinary skill in the pertinent art, when reading the claims in light of the content of the particular application's disclosure and the teachings of the prior art, would be able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the amended claims. *Ex parte* Wu, 10 USPQ 2d 2031, 2033 (B.P.A.I. 1989)(citing *In re* Moore, 439 F.2d 1232, 169 USPQ 236 (C.C.P.A. 1971); *In re* Hammack, 427 F.2d 1378, 166 USPQ 204 (C.C.P.A. 1970)). See *M.P.E.P.* § 2173.02.

Applicants also respectfully submit that the nucleotide sequence of plasmid of SEQ ID NO:1 is novel and the nucleotide sequence of the retroviral vector obtained from plasmid of SEQ ID NO:1 comprised in the tumor cell lines of the present invention is also novel. Thus, the claims are believed to be definite and patentable over the references made of record at least for the reasons set forth above, plus the elements in the claims. In light of the above, Applicants respectfully submit that the amended claims are in form for allowance.

III. Claim Rejections Under 35 U.S.C. § 103

A. Claims 1-4, 34, 67, 85, and 99 remain rejected under 35 U.S.C. 103(a) as allegedly being obvious over LaTemple-II (LaTemple-II, D. C. et al., Cancer Research, 56:3069-3074, 1996; cited in the IDS) in view of Link, Jr.-II (Link, Jr., et al., US 5,869,035 A; issued Feb. 9, 1999; of record), in view of Larsen (Larsen, R. D. et al., Proc. Natl. Acad. Sci, USA, 86:8277-8231, 1989), and further in view of ATCC (ATCC Cell Lines and Hybridomas, 8th edition, 1994, page 100; of record) for the reasons of record.

The Examiner writes that Link, Jr.-II is cited to provide a teaching of a specific nucleic acid molecule (SEQ ID NO:1), and a method for transforming a tumor cell line, not for its method of use of cells transformed with an α(1,3) galactosyltransferase encoding polynucleotide. The Examiner continues that Link, Jr.-II is included in the rejection to show that a polynucleotide sequence comprising the nucleotide sequence of SEQ ID NO:1 is in the prior art and has been used to transform tumor cells. The fact that Link, Jr.-II used the cell line in a different method than the method proposed in the present application for the claimed cells does not remove Link, Jr.-II as prior art because the claims are drawn to products which have not been shown to be structurally limited by an intended use.

Applicants disagree. To make an obviousness determination, section 2143.03 of the MPEP requires the "consideration" of every claim feature. LaTemple-II, Link, Jr.-II, Larsen and ATCC, individually or combined, fail to teach or suggest all the claim elements.

Independent claims 1, 2, 67 and 85 recite the vector of SEQ ID NO:1. U.S. Patent No. 5,869,035 describes an alphaGal vector that is different from the SEQ ID NO:1 in the instant claims. Even though the precise sequence is not available since restriction sites or PCR primers are not disclosed, U.S. Patent No. 5,869,035 states at Example 12, Col. 20, lines 44-47, "The α(1,3)GT gene was cloned into the pREP7 vector (Invitrogen) and then into the multi-cloning site of **LXSN** retroviral vector backbone (kindly provided by A. D. Miller, University of Washington) to generate the LαGTSN vector." (emphasis added). In contrast, the alphaGT truncated gene of SEQ ID NO: 1 was cloned into a different vector. The instant specification states at paragraph 141 of the published specification 20040191229: "A 1,077 bp fragment of murine αGT gene was PCR amplified by a forward primer, 5'-ACAAAAGCTTGACATGGATGTCAAGGGAAAAGTAAT-3', which contains a Kozak sequence to enhance the translation of αGT, and a reverse primer, 5'-AATTATCGATTCAGACATTATTTCTAAC-3', and then cloned into the ClaI and HindIII sites of **pLNCX** to produce pLNCKG retroviral vector (FIG. 1)." (emphasis added). Since the recipient vectors are different, it follows that the final nucleotide sequence is different. Further, the vector from the '035 patent uses a full-length αGal, while the one in the present application uses a truncated version of αGT. Accordingly, there is a difference between the nucleic acid of Link, Jr.-II and the nucleic acid in the present claims.

LaTemple-II, Larsen and ATCC do not teach the nucleotide of SEQ ID NO:1. Therefore, the § 103(a) rejection of claims 1-4, 34, 67, and 85 should be reconsidered and withdrawn. In light of the foregoing, Applicants respectfully submit that claims 1-4, 34, 67, 85, and 102 are in form for allowance.

B. Claims 1-4, 34, 66, 67, 85, 99, 102 and 103 remain/are rejected under 35 U.S.C. 103(a) as allegedly being obvious over LaTemple-II (LaTemple-II, D. C. et al, Cancer Research, 56:3069-3074, 1996; cited in the IDS) in view of Link, Jr.-II (Link, Jr., et al., US 5,869,035 A; issued Feb. 9, 1999; of record), in view of Larsen (Larsen, R. D. et al., Proc. Natl. Acad. Sci, USA, 86:8277-8231, 1989), in view of ATCC (ATCC Cell Lines and Hybridomas, 8th edition, 1994, page 100; of record), and further in view of Berd (US 6,333,028; issued Dec. 25, 2001; effective filing Aug. 14, 1998; of record) for the reasons of record. This rejection is applied to new claims 102 and 103.

Applicants disagree with the Examiner's conclusion that the claims are obvious. To make an obviousness determination, section 2143.03 of the MPEP requires the "consideration" of every claim feature. LaTemple-II, Link, Jr.-II, Larsen, ATCC, and Berd, individually or combined, fail to teach or suggest all the claim elements.

Independent claims 1, 2, 67, 85, and 102 recite the vector of SEQ ID NO:1. U.S. Patent No. 5,869,035 describes an alphaGal vector that is different from the SEQ ID NO:1 in the instant claims. Even though the precise sequence is not available since restriction sites or PCR primers are not disclosed, U.S. Patent No. 5,869,035 states at Example 12, Col. 20, lines 44-47, "The α(1,3)GT gene was cloned into the pREP7 vector (Invitrogen) and then into the multi-cloning site of **LXSN** retroviral vector backbone (kindly provided by A. D. Miller, University of Washington) to generate the LαGTSN vector." (emphasis added). In contrast, the alphaGT truncated gene of SEQ ID NO: 1 was cloned into a different vector. The instant specification states at paragraph 141 of the published specification 20040191229: "A 1,077 bp fragment of murine αGT gene was PCR amplified by a forward primer, 5'-

ACAAAAGCTTGACATGGATGTCAAGGGAAAAGTAAT-3', which contains a Kozak sequence to enhance the translation of αGT, and a reverse primer, 5'-AATTATCGATTCAGACATTATTTCTAAC-3', and then cloned into the ClaI and HindIII sites of **pLNCX** to produce pLNCKG retroviral vector (FIG. 1)." (emphasis added). Since the recipient vectors are different, it follows that the final nucleotide sequence is different. Further, the vector from the '035 patent uses a full-length αGal, while the one in the present application uses a truncated version of αGT. Accordingly, there is a difference between the nucleic acid of Link, Jr.-II and the nucleic acid in the present claims.

LaTemple-II, Larsen, ATCC, and Berd do not teach the vector of SEQ ID NO:1. Therefore, the § 103(a) rejection of claims 1-4, 34, 66, 67, 85, 102 and 103 should be reconsidered and withdrawn. In light of the foregoing, Applicants respectfully submit that claims 1-4, 34, 67, 85, and 102 are in form for allowance.

C. Claims 1-4, 34, 67, 85, and 99-103 remain/are rejected under 35 U.S.C. 103(a) as allegedly being obvious over LaTemple-II (LaTemple-II, D. C. et al, Cancer Research, 56:3069- 3074,1996; cited in the IDS) in view of Link, Jr.-II (Link, Jr., et al., US 5,869,035 A; issued Feb. 9, 1999; of record), in view of Larsen (Larsen, R. D. et al., Proc. Natl. Acad. Sci, USA, 86:8277-8231, 1989), in view of ATCC (ATCC Cell Lines and Hybridomas, 8th edition, 1994, page 100; of record), and further in view of Pardoll (US 6,187,306; Feb. 13,2001; effective filing date of Aug. 16, 1996) for the reasons of record.

Applicants disagree with the Examiner's conclusion that the claims are obvious. To make an obviousness determination, section 2143.03 of the MPEP requires the "consideration" of every claim feature. LaTemple-II, Link, Jr.-II, Larsen and ATCC, individually or combined, fail to teach or suggest all the claim elements.

Independent claims 1, 2, 67, 85, and 102 recite the vector of SEQ ID NO:1. U.S. Patent No. 5,869,035 describes an alphaGal vector that is different from the SEQ ID NO:1 in the instant claims. Even though the precise sequence is not available since restriction sites or PCR primers are not disclosed, U.S. Patent No. 5,869,035 states at Example 12, Col. 20, lines 44-47, "The α(1,3)GT gene was cloned into the pREP7 vector (Invitrogen) and then into the multi-cloning site of **LXSN** retroviral vector backbone (kindly provided by A. D. Miller, University of Washington) to generate the LαGTSN vector." (emphasis added). In contrast, the alphaGT truncated gene of SEQ ID NO: 1 was cloned into a different vector. The instant specification states at paragraph 141 of the published specification 20040191229: "A 1,077 bp fragment of murine αGT gene was PCR amplified by a forward primer, 5'-ACAAAAGCTTGACATGGATGTCAAGGGAAAAGTAAT-3', which contains a Kozak sequence to enhance the translation of αGT, and a reverse primer, 5'-AATTATCGATTCAGACATTATTTCTAAC-3', and then cloned into the ClaI and HindIII sites of **pLNCX** to produce pLNCKG retroviral vector (FIG. 1)." (emphasis added). Since the recipient vectors are different, it follows that the final nucleotide sequence is different. Further, the vector from the '035 patent uses a full-length αGal, while the one in the present application uses a truncated version of αGT. Accordingly, there is a difference between the nucleic acid of Link, Jr.-II and the nucleic acid in the present claims.

LaTemple-II, Larsen, ATCC, and Pardoll do not teach the vector of SEQ ID NO:1. Therefore, the § 103(a) rejection of claims 1-4, 34, 67, 85, and 100-103 should be reconsidered and withdrawn. In light of the foregoing, Applicants respectfully submit that claims 1-4, 34, 67, 85, and 100-103 are in form for allowance.

IV. Double Patenting

Claims 1-5, 66, 67, 68, 85 and 99-103 are/remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 11/013,685. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application no. 11/013,685 are drawn to a sub-genus of compositions encompassed by the claims of the instant application.

Applicant is herein submitting a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c), which disclaims any term of a patent issuing from this application which would extend beyond the term of copending U.S. Application No. 11/013,685 should it issue as a patent. Therefore, Applicant submits that the claims are in proper form for allowance and respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejection.

V. Conclusion

In the event that there are any questions relating to this response, Applicants invite the Examiner to call the undersigned attorney so that this case can be allowed.

This is a request to extend the period for filing a response in the above-identified application for two month from October 27, 2009 to December 27, 2009. Applicant is a small entity; therefore, please charge Deposit Account No. 26-0084 in the amount of $245.00 to cover the cost of the two month extension. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084 Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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